SEQUENCE LISTING

<110> Tanzi, Rudolph E.
Kovacs, Dora
Saunders, Aleister J.

<120> Alpha-2-Macroglobulin Therapies and Drug Screening Methods for Alzheimer's Disease

<130> 0609.4460005

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<150> 09/241,606
<151> 1999-02-02

<150> 09/148,503
<151> 1998-09-04

<150> 60/093,297
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Tyr Leu Asn Glu Thr Val Thr Val Ser Ala Ser Leu Glu Ser Val Arg
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Gly Asn Arg Ser Leu Phe Thr Asp Leu Glu Ala Glu Asn Asp Val Leu
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His Cys Val Ala Phe Ala Val Pro Lys Ser Ser Ser Asn Glu Glu Val
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atg ttc ctc act gtc caa gtg aaa gga cca acc caa gaa ttt aag aag   391
Met Phe Leu Thr Val Gln Val Lys Gly Pro Thr Gln Glu Phe Lys Lys
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cgg acc aca gtg atg gtt aag aac gag gac agt ctg gtc ttt gtc cag   439
Arg Thr Thr Val Met Val Lys Asn Glu Asp Ser Leu Val Phe Val Gln
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gta tac att cag gat ccc aaa gga aat cgc atc gca caa tgg cag agt   583
Val Tyr Ile Gln Asp Pro Lys Gly Asn Arg Ile Ala Gln Trp Gln Ser
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Phe Gln Leu Glu Gly Gly Leu Lys Gln Phe Ser Phe Pro Leu Ser Ser
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gag ccc ttc cag ggc tcc tac aag gtg gtg gta cag aag aaa tca ggt   679
Glu Pro Phe Gln Gly Ser Tyr Lys Val Val Val Gln Lys Lys Ser Gly
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gga agg aca gag cac cct ttc acc gtg gag gaa ttt gtt ctt ccc aag   727
Gly Arg Thr Glu His Pro Phe Thr Val Glu Glu Phe Val Leu Pro Lys
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Glu Met Asn Val Ser Val Cys Gly Leu Tyr Thr Tyr Gly Lys Pro Val
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cct gga cat gtg act gtg agc att tgc aga aag tat agt gac gct tcc   871
Pro Gly His Val Thr Val Ser Ile Cys Arg Lys Tyr Ser Asp Ala Ser
        240                 245                 250

gac tgc cac ggt gaa gat tca cag gct ttc tgt gag aaa ttc agt gga   919
Asp Cys His Gly Glu Asp Ser Gln Ala Phe Cys Glu Lys Phe Ser Gly
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cag cta aac agc cat ggc tgc ttc tat cag caa gta aaa acc aag gtc   967
Gln Leu Asn Ser His Gly Cys Phe Tyr Gln Gln Val Lys Thr Lys Val
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cag atc caa gaa gaa gga aca gtg gtg gaa ttg act gga agg cag tcc   1063
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agt gaa atc aca aga acc ata acc aaa ctc tca ttt gtg aaa gtg gac   1111
Ser Glu Ile Thr Arg Thr Ile Thr Lys Leu Ser Phe Val Lys Val Asp
        320                 325                 330

tca cac ttt cga cag gga att ccc ttc ttt ggg cag gtg cgc cta gta   1159
Ser His Phe Arg Gln Gly Ile Pro Phe Phe Gly Gln Val Arg Leu Val
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gat ggg aaa ggc gtc cct ata cca aat aaa gtc ata ttc atc aga gga   1207
Asp Gly Lys Gly Val Pro Ile Pro Asn Lys Val Ile Phe Ile Arg Gly
350                 355                 360                 365

aat gaa gca aac tat tac tcc aat gct acc acg gat gag cat ggc ctt   1255
Asn Glu Ala Asn Tyr Tyr Ser Asn Ala Thr Thr Asp Glu His Gly Leu
                370                 375                 380

gta cag ttc tct atc aac acc acc aac gtt atg ggt acc tct ctt act   1303
Val Gln Phe Ser Ile Asn Thr Thr Asn Val Met Gly Thr Ser Leu Thr
            385                 390                 395

gtt agg gtc aat tac aag gat cgt agt ccc tgt tac ggc tac cag tgg   1351
Val Arg Val Asn Tyr Lys Asp Arg Ser Pro Cys Tyr Gly Tyr Gln Trp
        400                 405                 410

gtg tca gaa gaa cac gaa gag gca cat cac act gct tat ctt gtg ttc   1399
Val Ser Glu Glu His Glu Glu Ala His His Thr Ala Tyr Leu Val Phe
    415                 420                 425

tcc cca agc aag agc ttt gtc cac ctt gag ccc atg tct cat gaa cta   1447
Ser Pro Ser Lys Ser Phe Val His Leu Glu Pro Met Ser His Glu Leu
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ccc tgt ggc cat act cag aca gtc cag gca cat tat att ctg aat gga   1495
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Pro Cys Gly His Thr Gln Thr Val Gln Ala His Tyr Ile Leu Asn Gly
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Gly Thr Leu Leu Gly Leu Lys Lys Leu Ser Phe Tyr Tyr Leu Ile Met
465 470 475

gca aag gga ggc att gtc cga act ggg act cat gga ctg ctt gtg aag 1591
Ala Lys Gly Gly Ile Val Arg Thr Gly Thr His Gly Leu Leu Val Lys
480 485 490

cag gaa gac atg aag ggc cat ttt tcc atc tca atc cct gtg aag tca 1639
Gln Glu Asp Met Lys Gly His Phe Ser Ile Ser Ile Pro Val Lys Ser
495 500 505

gac att gct cct gtc gct cgg ttg ctc atc tat gct gtt tta cct acc 1687
Asp Ile Ala Pro Val Ala Arg Leu Leu Ile Tyr Ala Val Leu Pro Thr
510 515 520 525

ggg gac gtg att ggg gat tct gca aaa tat gat gtt gaa aat tgt ctg 1735
Gly Asp Val Ile Gly Asp Ser Ala Lys Tyr Asp Val Glu Asn Cys Leu
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gcc aac aag gtg gat ttg agc ttc agc cca tca caa agt ctc cca gcc 1783
Ala Asn Lys Val Asp Leu Ser Phe Ser Pro Ser Gln Ser Leu Pro Ala
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Ser His Ala His Leu Arg Val Thr Ala Ala Pro Gln Ser Val Cys Ala
560 565 570

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Leu Arg Ala Val Asp Gln Ser Val Leu Leu Met Lys Pro Asp Ala Glu
575 580 585

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Leu Ser Ala Ser Ser Val Tyr Asn Leu Leu Pro Glu Lys Asp Leu Thr
590 595 600 605

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aca aat gaa aag gat atg tac agc ttc cta gag gac atg ggc tta aag   2071
Thr Asn Glu Lys Asp Met Tyr Ser Phe Leu Glu Asp Met Gly Leu Lys
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gca ttc acc aac tca aag att cgt aaa ccc aaa atg tgt cca cag ctt   2119
Ala Phe Thr Asn Ser Lys Ile Arg Lys Pro Lys Met Cys Pro Gln Leu
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caa cag tat gaa atg cat gga cct gaa ggt cta cgt gta ggt ttt tat   2167
Gln Gln Tyr Glu Met His Gly Pro Glu Gly Leu Arg Val Gly Phe Tyr
670                 675                 680                 685

gag tca gat gta atg gga aga ggc cat gca cgc ctg gtg cat gtt gaa   2215
Glu Ser Asp Val Met Gly Arg Gly His Ala Arg Leu Val His Val Glu
                690                 695                 700

gag cct cac acg gag acc gta cga aag tac ttc cct gag aca tgg atc   2263
Glu Pro His Thr Glu Thr Val Arg Lys Tyr Phe Pro Glu Thr Trp Ile
            705                 710                 715

tgg gat ttg gtg gtg gta aac tca gca ggg gtg gct gag gta gga gta   2311
Trp Asp Leu Val Val Val Asn Ser Ala Gly Val Ala Glu Val Gly Val
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aca gtc cct gac acc atc acc gag tgg aag gca ggg gcc ttc tgc ctg   2359
Thr Val Pro Asp Thr Ile Thr Glu Trp Lys Ala Gly Ala Phe Cys Leu
    735                 740                 745

tct gaa gat gct gga ctt ggt atc tct tcc act gcc tct ctc cga gcc   2407
Ser Glu Asp Ala Gly Leu Gly Ile Ser Ser Thr Ala Ser Leu Arg Ala
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Gly Glu Ala Phe Thr Leu Lys Ala Thr Val Leu Asn Tyr Leu Pro Lys
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tgc atc cgg gtc agt gtg cag ctg gaa gcc tct ccc gcc ttc ctt gct    2551
Cys Ile Arg Val Ser Val Gln Leu Glu Ala Ser Pro Ala Phe Leu Ala
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gtc cca gtg gag aag gaa caa gcg cct cac tgc atc tgt gca aac ggg    2599
Val Pro Val Glu Lys Glu Gln Ala Pro His Cys Ile Cys Ala Asn Gly
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cgg caa act gtg tcc tgg gca gta acc cca aag tca tta gga aat gtg    2647
Arg Gln Thr Val Ser Trp Ala Val Thr Pro Lys Ser Leu Gly Asn Val
830                 835                 840                 845

aat ttc act gtg agc gca gag gca cta gag tct caa gag ctg tgt ggg    2695
Asn Phe Thr Val Ser Ala Glu Ala Leu Glu Ser Gln Glu Leu Cys Gly
                850                 855                 860

act gag gtg cct tca gtt cct gaa cac gga agg aaa gac aca gtc atc    2743
Thr Glu Val Pro Ser Val Pro Glu His Gly Arg Lys Asp Thr Val Ile
            865                 870                 875

aag cct ctg ttg gtt gaa cct gaa gga cta gag aag gaa aca aca ttc    2791
Lys Pro Leu Leu Val Glu Pro Glu Gly Leu Glu Lys Glu Thr Thr Phe
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aac tcc cta ctt tgt cca tca ggt ggt gag gtt tct gaa gaa tta tcc    2839
Asn Ser Leu Leu Cys Pro Ser Gly Gly Glu Val Ser Glu Glu Leu Ser
    895                 900                 905

ctg aaa ctg cca cca aat gtg gta gaa gaa tct gcc cga gct tct gtc    2887
Leu Lys Leu Pro Pro Asn Val Val Glu Glu Ser Ala Arg Ala Ser Val
910                 915                 920                 925

tca gtt ttg gga gac ata tta ggc tct gcc atg caa aac aca caa aat    2935
Ser Val Leu Gly Asp Ile Leu Gly Ser Ala Met Gln Asn Thr Gln Asn
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gct cct aac atc tat gta ctg gat tat cta aat gaa aca cag cag ctt   3031
Ala Pro Asn Ile Tyr Val Leu Asp Tyr Leu Asn Glu Thr Gln Gln Leu
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act cca gag atc aag tcc aag gcc att ggc tat ctc aac act ggt tac   3079
Thr Pro Glu Ile Lys Ser Lys Ala Ile Gly Tyr Leu Asn Thr Gly Tyr
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cag aga cag ttg aac tac aaa cac tat gat ggc tcc tac agc acc ttt   3127
Gln Arg Gln Leu Asn Tyr Lys His Tyr Asp Gly Ser Tyr Ser Thr Phe
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ggg gag cga tat ggc agg aac cag ggc aac acc tgg ctc aca gcc ttt   3175
Gly Glu Arg Tyr Gly Arg Asn Gln Gly Asn Thr Trp Leu Thr Ala Phe
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Val Leu Lys Thr Phe Ala Gln Ala Arg Ala Tyr Ile Phe Ile Asp Glu
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Ala His Ile Thr Gln Ala Leu Ile Trp Leu Ser Gln Arg Gln Lys Asp
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aat ggc tgt ttc agg agc tct ggg tca ctg ctc aac aat gcc ata aag   3319
Asn Gly Cys Phe Arg Ser Ser Gly Ser Leu Leu Asn Asn Ala Ile Lys
   1055                1060                1065

gga gga gta gaa gat gaa gtg acc ctc tcc gcc tat atc acc atc gcc   3367
Gly Gly Val Glu Asp Glu Val Thr Leu Ser Ala Tyr Ile Thr Ile Ala
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ctt ctg gag att cct ctc aca gtc act cac cct gtt gtc cgc aat gcc   3415
Leu Leu Glu Ile Pro Leu Thr Val Thr His Pro Val Val Arg Asn Ala
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ctg ttt tgc ctg gag tca gcc tgg aag aca gca caa gaa ggg gac cat   3463
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Gly Ser His Val Tyr Thr Lys Ala Leu Leu Ala Tyr Ala Phe Ala Leu
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gca ggt aac cag gac aag agg aag gaa gta ctc aag tca ctt aat gag   3559
Ala Gly Asn Gln Asp Lys Arg Lys Glu Val Leu Lys Ser Leu Asn Glu
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gaa gct gtg aag aaa gac aac tct gtc cat tgg gag cgc cct cag aaa   3607
Glu Ala Val Lys Lys Asp Asn Ser Val His Trp Glu Arg Pro Gln Lys
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ccc aag gca cca gtg ggg cat ttt tac gaa ccc cag gct ccc tct gct   3655
Pro Lys Ala Pro Val Gly His Phe Tyr Glu Pro Gln Ala Pro Ser Ala
               1170                1175                1180

gag gtg gag atg aca tcc tat gtg ctc ctc gct tat ctc acg gcc cag   3703
Glu Val Glu Met Thr Ser Tyr Val Leu Leu Ala Tyr Leu Thr Ala Gln
          1185                1190                1195

cca gcc cca acc tcg gag gac ctg acc tct gca acc aac atc gtg aag   3751
Pro Ala Pro Thr Ser Glu Asp Leu Thr Ser Ala Thr Asn Ile Val Lys
       1200                1205                1210

tgg atc acg aag cag cag aat gcc cag ggc ggt ttc tcc tcc acc cag   3799
Trp Ile Thr Lys Gln Gln Asn Ala Gln Gly Gly Phe Ser Ser Thr Gln
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gac aca gtg gtg gct ctc cat gct ctg tcc aaa tat gga gcc gcc aca   3847
Asp Thr Val Val Ala Leu His Ala Leu Ser Lys Tyr Gly Ala Ala Thr
1230                1235                1240                1245

ttt acc agg act ggg aag gct gca cag gtg act atc cag tct tca ggg   3895
Phe Thr Arg Thr Gly Lys Ala Ala Gln Val Thr Ile Gln Ser Ser Gly
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aca ttt tcc agc aaa ttc caa gtg gac aac aac aat cgc ctg tta ctg   3943
Thr Phe Ser Ser Lys Phe Gln Val Asp Asn Asn Asn Arg Leu Leu Leu
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aca gga gaa gga tgt gtc tac ctc cag acc tcc ttg aaa tac aat att   4039
Thr Gly Glu Gly Cys Val Tyr Leu Gln Thr Ser Leu Lys Tyr Asn Ile
   1295                1300                1305

ctc cca gaa aag gaa gag ttc ccc ttt gct tta gga gtg cag act ctg   4087
Leu Pro Glu Lys Glu Glu Phe Pro Phe Ala Leu Gly Val Gln Thr Leu
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cct caa act tgt gat gaa ccc aaa gcc cac acc agc ttc caa atc tcc   4135
Pro Gln Thr Cys Asp Glu Pro Lys Ala His Thr Ser Phe Gln Ile Ser
               1330                1335                1340

cta agt gtc agt tac aca ggg agc cgc tct gcc tcc aac atg gcg atc   4183
Leu Ser Val Ser Tyr Thr Gly Ser Arg Ser Ala Ser Asn Met Ala Ile
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gtt gat gtg aag atg gtc tct ggc ttc att ccc ctg aag cca aca gtg   4231
Val Asp Val Lys Met Val Ser Gly Phe Ile Pro Leu Lys Pro Thr Val
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aaa atg ctt gaa aga tct aac cat gtg agc cgg aca gaa gtc agc agc   4279
Lys Met Leu Glu Arg Ser Asn His Val Ser Arg Thr Glu Val Ser Ser
   1375                1380                1385

aac cat gtc ttg att tac ctt gat aag gtg tca aat cag aca ctg agc   4327
Asn His Val Leu Ile Tyr Leu Asp Lys Val Ser Asn Gln Thr Leu Ser
1390                1395                1400                1405

ttg ttc ttc acg gtt ctg caa gat gtc cca gta aga gat ctc aaa cca   4375
Leu Phe Phe Thr Val Leu Gln Asp Val Pro Val Arg Asp Leu Lys Pro
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gcc ata gtg aaa gtc tat gat tac tac gag acg gat gag ttt gca atc   4423
Ala Ile Val Lys Val Tyr Asp Tyr Tyr Glu Thr Asp Glu Phe Ala Ile
          1425                1430                1435
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35 40 45

Val Leu Leu Ser Tyr Leu Asn Glu Thr Val Thr Val Ser Ala Ser Leu
50 55 60

Glu Ser Val Arg Gly Asn Arg Ser Leu Phe Thr Asp Leu Glu Ala Glu
65 70 75 80

Asn Asp Val Leu His Cys Val Ala Phe Ala Val Pro Lys Ser Ser Ser
85 90 95

Asn Glu Glu Val Met Phe Leu Thr Val Gln Val Lys Gly Pro Thr Gln
100 105 110

Glu Phe Lys Lys Arg Thr Thr Val Met Val Lys Asn Glu Asp Ser Leu
115 120 125

Val Phe Val Gln Thr Asp Lys Ser Ile Tyr Lys Pro Gly Gln Thr Val

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Lys Phe Arg Val Val Ser Met Asp Glu Asn Phe His Pro Leu Asn Glu
145                 150                 155                 160

Leu Ile Pro Leu Val Tyr Ile Gln Asp Pro Lys Gly Asn Arg Ile Ala
                165                 170                 175

Gln Trp Gln Ser Phe Gln Leu Glu Gly Gly Leu Lys Gln Phe Ser Phe
            180                 185                 190

Pro Leu Ser Ser Glu Pro Phe Gln Gly Ser Tyr Lys Val Val Val Gln
        195                 200                 205

Lys Lys Ser Gly Gly Arg Thr Glu His Pro Phe Thr Val Glu Glu Phe
    210                 215                 220

Val Leu Pro Lys Phe Glu Val Gln Val Thr Val Pro Lys Ile Ile Thr
225                 230                 235                 240

Ile Leu Glu Glu Glu Met Asn Val Ser Val Cys Gly Leu Tyr Thr Tyr
                245                 250                 255

Gly Lys Pro Val Pro Gly His Val Thr Val Ser Ile Cys Arg Lys Tyr
            260                 265                 270

Ser Asp Ala Ser Asp Cys His Gly Glu Asp Ser Gln Ala Phe Cys Glu
        275                 280                 285

Lys Phe Ser Gly Gln Leu Asn Ser His Gly Cys Phe Tyr Gln Gln Val
    290                 295                 300

Lys Thr Lys Val Phe Gln Leu Lys Arg Lys Glu Tyr Glu Met Lys Leu
305                 310                 315                 320

His Thr Glu Ala Gln Ile Gln Glu Glu Gly Thr Val Val Glu Leu Thr
                325                 330                 335

Gly Arg Gln Ser Ser Glu Ile Thr Arg Thr Ile Thr Lys Leu Ser Phe
            340                 345                 350
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Val Lys Val Asp Ser His Phe Arg Gln Gly Ile Pro Phe Phe Gly Gln
        355                 360                 365

Val Arg Leu Val Asp Gly Lys Gly Val Pro Ile Pro Asn Lys Val Ile
    370                 375                 380

Phe Ile Arg Gly Asn Glu Ala Asn Tyr Tyr Ser Asn Ala Thr Thr Asp
385                 390                 395                 400

Glu His Gly Leu Val Gln Phe Ser Ile Asn Thr Thr Asn Val Met Gly
                405                 410                 415

Thr Ser Leu Thr Val Arg Val Asn Tyr Lys Asp Arg Ser Pro Cys Tyr
            420                 425                 430

Gly Tyr Gln Trp Val Ser Glu Glu His Glu Glu Ala His His Thr Ala
        435                 440                 445

Tyr Leu Val Phe Ser Pro Ser Lys Ser Phe Val His Leu Glu Pro Met
    450                 455                 460

Ser His Glu Leu Pro Cys Gly His Thr Gln Thr Val Gln Ala His Tyr
465                 470                 475                 480

Ile Leu Asn Gly Gly Thr Leu Leu Gly Leu Lys Lys Leu Ser Phe Tyr
                485                 490                 495

Tyr Leu Ile Met Ala Lys Gly Gly Ile Val Arg Thr Gly Thr His Gly
            500                 505                 510

Leu Leu Val Lys Gln Glu Asp Met Lys Gly His Phe Ser Ile Ser Ile
        515                 520                 525

Pro Val Lys Ser Asp Ile Ala Pro Val Ala Arg Leu Leu Ile Tyr Ala
    530                 535                 540

Val Leu Pro Thr Gly Asp Val Ile Gly Asp Ser Ala Lys Tyr Asp Val
545                 550                 555                 560

Glu Asn Cys Leu Ala Asn Lys Val Asp Leu Ser Phe Ser Pro Ser Gln
                565                 570                 575
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Ser Leu Pro Ala Ser His Ala His Leu Arg Val Thr Ala Ala Pro Gln
            580                 585                 590

Ser Val Cys Ala Leu Arg Ala Val Asp Gln Ser Val Leu Leu Met Lys
        595                 600                 605

Pro Asp Ala Glu Leu Ser Ala Ser Ser Val Tyr Asn Leu Leu Pro Glu
    610                 615                 620

Lys Asp Leu Thr Gly Phe Pro Gly Pro Leu Asn Asp Gln Asp Asp Glu
625                 630                 635                 640

Asp Cys Ile Asn Arg His Asn Val Tyr Ile Asn Gly Ile Thr Tyr Thr
                645                 650                 655

Pro Val Ser Ser Thr Asn Glu Lys Asp Met Tyr Ser Phe Leu Glu Asp
            660                 665                 670

Met Gly Leu Lys Ala Phe Thr Asn Ser Lys Ile Arg Lys Pro Lys Met
        675                 680                 685

Cys Pro Gln Leu Gln Gln Tyr Glu Met His Gly Pro Glu Gly Leu Arg
    690                 695                 700

Val Gly Phe Tyr Glu Ser Asp Val Met Gly Arg Gly His Ala Arg Leu
705                 710                 715                 720

Val His Val Glu Glu Pro His Thr Glu Thr Val Arg Lys Tyr Phe Pro
                725                 730                 735

Glu Thr Trp Ile Trp Asp Leu Val Val Val Asn Ser Ala Gly Val Ala
            740                 745                 750

Glu Val Gly Val Thr Val Pro Asp Thr Ile Thr Glu Trp Lys Ala Gly
        755                 760                 765

Ala Phe Cys Leu Ser Glu Asp Ala Gly Leu Gly Ile Ser Ser Thr Ala
    770                 775                 780

Ser Leu Arg Ala Phe Gln Pro Phe Phe Val Glu Leu Thr Met Pro Tyr
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785 790 795 800

Ser Val Ile Arg Gly Glu Ala Phe Thr Leu Lys Ala Thr Val Leu Asn
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Tyr Leu Pro Lys Cys Ile Arg Val Ser Val Gln Leu Glu Ala Ser Pro
820 825 830

Ala Phe Leu Ala Val Pro Val Glu Lys Glu Gln Ala Pro His Cys Ile
835 840 845

Cys Ala Asn Gly Arg Gln Thr Val Ser Trp Ala Val Thr Pro Lys Ser
850 855 860

Leu Gly Asn Val Asn Phe Thr Val Ser Ala Glu Ala Leu Glu Ser Gln
865 870 875 880

Glu Leu Cys Gly Thr Glu Val Pro Ser Val Pro Glu His Gly Arg Lys
885 890 895

Asp Thr Val Ile Lys Pro Leu Leu Val Glu Pro Glu Gly Leu Glu Lys
900 905 910

Glu Thr Thr Phe Asn Ser Leu Leu Cys Pro Ser Gly Gly Glu Val Ser
915 920 925

Glu Glu Leu Ser Leu Lys Leu Pro Pro Asn Val Val Glu Glu Ser Ala
930 935 940

Arg Ala Ser Val Ser Val Leu Gly Asp Ile Leu Gly Ser Ala Met Gln
945 950 955 960

Asn Thr Gln Asn Leu Leu Gln Met Pro Tyr Gly Cys Gly Glu Gln Asn
965 970 975

Met Val Leu Phe Ala Pro Asn Ile Tyr Val Leu Asp Tyr Leu Asn Glu
980 985 990

Thr Gln Gln Leu Thr Pro Glu Ile Lys Ser Lys Ala Ile Gly Tyr Leu
995 1000 1005

Asn Thr Gly Tyr Gln Arg Gln Leu Asn Tyr Lys His Tyr Asp Gly Ser
1010 1015 1020

Tyr Ser Thr Phe Gly Glu Arg Tyr Gly Arg Asn Gln Gly Asn Thr Trp
1025 1030 1035 1040

Leu Thr Ala Phe Val Leu Lys Thr Phe Ala Gln Ala Arg Ala Tyr Ile
1045 1050 1055

Phe Ile Asp Glu Ala His Ile Thr Gln Ala Leu Ile Trp Leu Ser Gln
1060 1065 1070

Arg Gln Lys Asp Asn Gly Cys Phe Arg Ser Ser Gly Ser Leu Leu Asn
1075 1080 1085

Asn Ala Ile Lys Gly Gly Val Glu Asp Glu Val Thr Leu Ser Ala Tyr
1090 1095 1100

Ile Thr Ile Ala Leu Leu Glu Ile Pro Leu Thr Val Thr His Pro Val
1105 1110 1115 1120

Val Arg Asn Ala Leu Phe Cys Leu Glu Ser Ala Trp Lys Thr Ala Gln
1125 1130 1135

Glu Gly Asp His Gly Ser His Val Tyr Thr Lys Ala Leu Leu Ala Tyr
1140 1145 1150

Ala Phe Ala Leu Ala Gly Asn Gln Asp Lys Arg Lys Glu Val Leu Lys
1155 1160 1165

Ser Leu Asn Glu Glu Ala Val Lys Lys Asp Asn Ser Val His Trp Glu
1170 1175 1180

Arg Pro Gln Lys Pro Lys Ala Pro Val Gly His Phe Tyr Glu Pro Gln
1185 1190 1195 1200

Ala Pro Ser Ala Glu Val Glu Met Thr Ser Tyr Val Leu Leu Ala Tyr
1205 1210 1215

Leu Thr Ala Gln Pro Ala Pro Thr Ser Glu Asp Leu Thr Ser Ala Thr
1220 1225 1230

Asn Ile Val Lys Trp Ile Thr Lys Gln Gln Asn Ala Gln Gly Gly Phe
1235 1240 1245

Ser Ser Thr Gln Asp Thr Val Val Ala Leu His Ala Leu Ser Lys Tyr
1250 1255 1260

Gly Ala Ala Thr Phe Thr Arg Thr Gly Lys Ala Ala Gln Val Thr Ile
1265 1270 1275 1280

Gln Ser Ser Gly Thr Phe Ser Ser Lys Phe Gln Val Asp Asn Asn Asn
1285 1290 1295

Arg Leu Leu Leu Gln Gln Val Ser Leu Pro Glu Leu Pro Gly Glu Tyr
1300 1305 1310

Ser Met Lys Val Thr Gly Glu Gly Cys Val Tyr Leu Gln Thr Ser Leu
1315 1320 1325

Lys Tyr Asn Ile Leu Pro Glu Lys Glu Glu Phe Pro Phe Ala Leu Gly
1330 1335 1340

Val Gln Thr Leu Pro Gln Thr Cys Asp Glu Pro Lys Ala His Thr Ser
1345 1350 1355 1360

Phe Gln Ile Ser Leu Ser Val Ser Tyr Thr Gly Ser Arg Ser Ala Ser
1365 1370 1375

Asn Met Ala Ile Val Asp Val Lys Met Val Ser Gly Phe Ile Pro Leu
1380 1385 1390

Lys Pro Thr Val Lys Met Leu Glu Arg Ser Asn His Val Ser Arg Thr
1395 1400 1405

Glu Val Ser Ser Asn His Val Leu Ile Tyr Leu Asp Lys Val Ser Asn
1410 1415 1420

Gln Thr Leu Ser Leu Phe Phe Thr Val Leu Gln Asp Val Pro Val Arg
1425 1430 1435 1440

Asp Leu Lys Pro Ala Ile Val Lys Val Tyr Asp Tyr Tyr Glu Thr Asp

1445 1450 1455

Glu Phe Ala Ile Ala Glu Tyr Asn Ala Pro Cys Ser Lys Asp Leu Gly
1460 1465 1470

Asn Ala

<210> 3
<211> 750
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(750)
<223> Aβ/LRP Binding Domain

<400> 3

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tcg gag gac ctg acc tct gca acc aac atc gtg aag tgg atc acg aag   48
Ser Glu Asp Leu Thr Ser Ala Thr Asn Ile Val Lys Trp Ile Thr Lys
  1               5                  10                  15

cag cag aat gcc cag ggc ggt ttc tcc tcc acc cag gac aca gtg gtg   96
Gln Gln Asn Ala Gln Gly Gly Phe Ser Ser Thr Gln Asp Thr Val Val
             20                  25                  30

gct ctc cat gct ctg tcc aaa tat gga gcc gcc aca ttt acc agg act  144
Ala Leu His Ala Leu Ser Lys Tyr Gly Ala Ala Thr Phe Thr Arg Thr
         35                  40                  45

ggg aag gct gca cag gtg act atc cag tct tca ggg aca ttt tcc agc  192
Gly Lys Ala Ala Gln Val Thr Ile Gln Ser Ser Gly Thr Phe Ser Ser
     50                  55                  60

aaa ttc caa gtg gac aac aac aat cgc ctg tta ctg cag cag gtc tca  240
Lys Phe Gln Val Asp Asn Asn Asn Arg Leu Leu Leu Gln Gln Val Ser
 65                  70                  75                  80

ttg cca gag ctg cct ggg gaa tac agc atg aaa gtg aca gga gaa gga  288
Leu Pro Glu Leu Pro Gly Glu Tyr Ser Met Lys Val Thr Gly Glu Gly
```

```
                 85                  90                  95

tgt gtc tac ctc cag acc tcc ttg aaa tac aat att ctc cca gaa aag     336
Cys Val Tyr Leu Gln Thr Ser Leu Lys Tyr Asn Ile Leu Pro Glu Lys
            100                 105                 110

gaa gag ttc ccc ttt gct tta gga gtg cag act ctg cct caa act tgt     384
Glu Glu Phe Pro Phe Ala Leu Gly Val Gln Thr Leu Pro Gln Thr Cys
        115                 120                 125

gat gaa ccc aaa gcc cac acc agc ttc caa atc tcc cta agt gtc agt     432
Asp Glu Pro Lys Ala His Thr Ser Phe Gln Ile Ser Leu Ser Val Ser
    130                 135                 140

tac aca ggg agc cgc tct gcc tcc aac atg gcg atc gtt gat gtg aag     480
Tyr Thr Gly Ser Arg Ser Ala Ser Asn Met Ala Ile Val Asp Val Lys
145                 150                 155                 160

atg gtc tct ggc ttc att ccc ctg aag cca aca gtg aaa atg ctt gaa     528
Met Val Ser Gly Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu Glu
                165                 170                 175

aga tct aac cat gtg agc cgg aca gaa gtc agc agc aac cat gtc ttg     576
Arg Ser Asn His Val Ser Arg Thr Glu Val Ser Ser Asn His Val Leu
            180                 185                 190

att tac ctt gat aag gtg tca aat cag aca ctg agc ttg ttc ttc acg     624
Ile Tyr Leu Asp Lys Val Ser Asn Gln Thr Leu Ser Leu Phe Phe Thr
        195                 200                 205

gtt ctg caa gat gtc cca gta aga gat ctc aaa cca gcc ata gtg aaa     672
Val Leu Gln Asp Val Pro Val Arg Asp Leu Lys Pro Ala Ile Val Lys
    210                 215                 220

gtc tat gat tac tac gag acg gat gag ttt gca atc gct gag tac aat     720
Val Tyr Asp Tyr Tyr Glu Thr Asp Glu Phe Ala Ile Ala Glu Tyr Asn
225                 230                 235                 240

gct cct tgc agc aaa gat ctt gga aat gct                             750
Ala Pro Cys Ser Lys Asp Leu Gly Asn Ala
                245                 250
```

<210> 4
<211> 250
<212> PRT
<213> Homo sapiens

<400> 4

Ser Glu Asp Leu Thr Ser Ala Thr Asn Ile Val Lys Trp Ile Thr Lys
1   5   10   15

Gln Gln Asn Ala Gln Gly Gly Phe Ser Ser Thr Gln Asp Thr Val Val
            20   25   30

Ala Leu His Ala Leu Ser Lys Tyr Gly Ala Ala Thr Phe Thr Arg Thr
        35   40   45

Gly Lys Ala Ala Gln Val Thr Ile Gln Ser Ser Gly Thr Phe Ser Ser
    50   55   60

Lys Phe Gln Val Asp Asn Asn Asn Arg Leu Leu Leu Gln Gln Val Ser
65   70   75   80

Leu Pro Glu Leu Pro Gly Glu Tyr Ser Met Lys Val Thr Gly Glu Gly
                85   90   95

Cys Val Tyr Leu Gln Thr Ser Leu Lys Tyr Asn Ile Leu Pro Glu Lys
            100   105   110

Glu Glu Phe Pro Phe Ala Leu Gly Val Gln Thr Leu Pro Gln Thr Cys
        115   120   125

Asp Glu Pro Lys Ala His Thr Ser Phe Gln Ile Ser Leu Ser Val Ser
    130   135   140

Tyr Thr Gly Ser Arg Ser Ala Ser Asn Met Ala Ile Val Asp Val Lys
145   150   155   160

Met Val Ser Gly Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu Glu
                165   170   175

Arg Ser Asn His Val Ser Arg Thr Glu Val Ser Ser Asn His Val Leu
180 185 190

Ile Tyr Leu Asp Lys Val Ser Asn Gln Thr Leu Ser Leu Phe Phe Thr
195 200 205

Val Leu Gln Asp Val Pro Val Arg Asp Leu Lys Pro Ala Ile Val Lys
210 215 220

Val Tyr Asp Tyr Tyr Glu Thr Asp Glu Phe Ala Ile Ala Glu Tyr Asn
225 230 235 240

Ala Pro Cys Ser Lys Asp Leu Gly Asn Ala
245 250

<210> 5
<211> 333
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(333)
<223> Aβ Binding Domain

<400> 5
tcg gag gac ctg acc tct gca acc aac atc gtg aag tgg atc acg aag 48
Ser Glu Asp Leu Thr Ser Ala Thr Asn Ile Val Lys Trp Ile Thr Lys
1 5 10 15

cag cag aat gcc cag ggc ggt ttc tcc tcc acc cag gac aca gtg gtg 96
Gln Gln Asn Ala Gln Gly Gly Phe Ser Ser Thr Gln Asp Thr Val Val
20 25 30

gct ctc cat gct ctg tcc aaa tat gga gcc gcc aca ttt acc agg act 144
Ala Leu His Ala Leu Ser Lys Tyr Gly Ala Ala Thr Phe Thr Arg Thr
35 40 45

ggg aag gct gca cag gtg act atc cag tct tca ggg aca ttt tcc agc 192
Gly Lys Ala Ala Gln Val Thr Ile Gln Ser Ser Gly Thr Phe Ser Ser

```
     50                  55                  60

aaa ttc caa gtg gac aac aac aat cgc ctg tta ctg cag cag gtc tca   240
Lys Phe Gln Val Asp Asn Asn Asn Arg Leu Leu Leu Gln Gln Val Ser
 65                  70                  75                  80

ttg cca gag ctg cct ggg gaa tac agc atg aaa gtg aca gga gaa gga   288
Leu Pro Glu Leu Pro Gly Glu Tyr Ser Met Lys Val Thr Gly Glu Gly
                85                  90                  95

tgt gtc tac ctc cag acc tcc ttg aaa tac aat att ctc cca gaa       333
Cys Val Tyr Leu Gln Thr Ser Leu Lys Tyr Asn Ile Leu Pro Glu
            100                 105                 110
```


<210> 6
<211> 111
<212> PRT
<213> Homo sapiens

<400> 6

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Ser Glu Asp Leu Thr Ser Ala Thr Asn Ile Val Lys Trp Ile Thr Lys
  1               5                  10                  15

Gln Gln Asn Ala Gln Gly Gly Phe Ser Ser Thr Gln Asp Thr Val Val
             20                  25                  30

Ala Leu His Ala Leu Ser Lys Tyr Gly Ala Ala Thr Phe Thr Arg Thr
         35                  40                  45

Gly Lys Ala Ala Gln Val Thr Ile Gln Ser Ser Gly Thr Phe Ser Ser
     50                  55                  60

Lys Phe Gln Val Asp Asn Asn Asn Arg Leu Leu Leu Gln Gln Val Ser
 65                  70                  75                  80

Leu Pro Glu Leu Pro Gly Glu Tyr Ser Met Lys Val Thr Gly Glu Gly
                85                  90                  95

Cys Val Tyr Leu Gln Thr Ser Leu Lys Tyr Asn Ile Leu Pro Glu
            100                 105                 110
```

<210> 7
<211> 417
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(417)
<223> LRP Binding Domain

<400> 7

```
aag gaa gag ttc ccc ttt gct tta gga gtg cag act ctg cct caa act   48
Lys Glu Glu Phe Pro Phe Ala Leu Gly Val Gln Thr Leu Pro Gln Thr
  1               5                  10                  15

tgt gat gaa ccc aaa gcc cac acc agc ttc caa atc tcc cta agt gtc   96
Cys Asp Glu Pro Lys Ala His Thr Ser Phe Gln Ile Ser Leu Ser Val
             20                  25                  30

agt tac aca ggg agc cgc tct gcc tcc aac atg gcg atc gtt gat gtg   144
Ser Tyr Thr Gly Ser Arg Ser Ala Ser Asn Met Ala Ile Val Asp Val
         35                  40                  45

aag atg gtc tct ggc ttc att ccc ctg aag cca aca gtg aaa atg ctt   192
Lys Met Val Ser Gly Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu
     50                  55                  60

gaa aga tct aac cat gtg agc cgg aca gaa gtc agc agc aac cat gtc   240
Glu Arg Ser Asn His Val Ser Arg Thr Glu Val Ser Ser Asn His Val
 65                  70                  75                  80

ttg att tac ctt gat aag gtg tca aat cag aca ctg agc ttg ttc ttc   288
Leu Ile Tyr Leu Asp Lys Val Ser Asn Gln Thr Leu Ser Leu Phe Phe
                 85                  90                  95

acg gtt ctg caa gat gtc cca gta aga gat ctc aaa cca gcc ata gtg   336
Thr Val Leu Gln Asp Val Pro Val Arg Asp Leu Lys Pro Ala Ile Val
            100                 105                 110
```

```
aaa gtc tat gat tac tac gag acg gat gag ttt gca atc gct gag tac   384
Lys Val Tyr Asp Tyr Tyr Glu Thr Asp Glu Phe Ala Ile Ala Glu Tyr
        115                 120                 125

aat gct cct tgc agc aaa gat ctt gga aat gct                      417
Asn Ala Pro Cys Ser Lys Asp Leu Gly Asn Ala
    130                 135
```


<210> 8
<211> 139
<212> PRT
<213> Homo sapiens

<400> 8

```
Lys Glu Glu Phe Pro Phe Ala Leu Gly Val Gln Thr Leu Pro Gln Thr
  1               5                  10                  15

Cys Asp Glu Pro Lys Ala His Thr Ser Phe Gln Ile Ser Leu Ser Val
             20                  25                  30

Ser Tyr Thr Gly Ser Arg Ser Ala Ser Asn Met Ala Ile Val Asp Val
         35                  40                  45

Lys Met Val Ser Gly Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu
     50                  55                  60

Glu Arg Ser Asn His Val Ser Arg Thr Glu Val Ser Ser Asn His Val
 65                  70                  75                  80

Leu Ile Tyr Leu Asp Lys Val Ser Asn Gln Thr Leu Ser Leu Phe Phe
                 85                  90                  95

Thr Val Leu Gln Asp Val Pro Val Arg Asp Leu Lys Pro Ala Ile Val
            100                 105                 110

Lys Val Tyr Asp Tyr Tyr Glu Thr Asp Glu Phe Ala Ile Ala Glu Tyr
        115                 120                 125

Asn Ala Pro Cys Ser Lys Asp Leu Gly Asn Ala
    130                 135
```

<210> 9
<211> 81
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(81)
<223> Consensus LRP Binding Domain

<400> 9
ttc att ccc ctg aag cca aca gtg aaa atg ctt gaa aga tct aac cat 48
Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu Glu Arg Ser Asn His
1 5 10 15

gtg agc cgg aca gaa gtc agc agc aac cat gtc 81
Val Ser Arg Thr Glu Val Ser Ser Asn His Val
20 25

<210> 10
<211> 27
<212> PRT
<213> Homo sapiens

<400> 10
Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu Glu Arg Ser Asn His
1 5 10 15

Val Ser Arg Thr Glu Val Ser Ser Asn His Val
20 25

<210> 11
<211> 33
<212> DNA
<213> Homo sapiens

<220>

<221> CDS
<222> (1)..(33)
<223> Aβ Fibril Inhibitor

<400> 11
cgc gat ctg cca ttc ttc cca gtc cca att gat 33
Arg Asp Leu Pro Phe Phe Pro Val Pro Ile Asp
1 5 10

<210> 12
<211> 11
<212> PRT
<213> Homo sapiens

<400> 12
Arg Asp Leu Pro Phe Phe Pro Val Pro Ile Asp
1 5 10

<210> 13
<211> 114
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(114)
<223> Aβ Fibril Inhibitor

<400> 13
cgc gat ctg cca ttc ttc cca gtc cca att gat ttc att ccc ctg aag 48
Arg Asp Leu Pro Phe Phe Pro Val Pro Ile Asp Phe Ile Pro Leu Lys
1 5 10 15

cca aca gtg aaa atg ctt gaa aga tct aac cat gtg agc cgg aca gaa 96
Pro Thr Val Lys Met Leu Glu Arg Ser Asn His Val Ser Arg Thr Glu
20 25 30

gtc agc agc aac cat gtc 114
Val Ser Ser Asn His Val

35

<210> 14
<211> 38
<212> PRT
<213> Homo sapiens

<400> 14
Arg Asp Leu Pro Phe Phe Pro Val Pro Ile Asp Phe Ile Pro Leu Lys
1 5 10 15

Pro Thr Val Lys Met Leu Glu Arg Ser Asn His Val Ser Arg Thr Glu
20 25 30

Val Ser Ser Asn His Val
35

<210> 15
<211> 27
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(27)

<400> 15
cgc gat ctg cca ttc ttc cca gtc gat 27
Arg Asp Leu Pro Phe Phe Pro Val Asp
1 5

<210> 16
<211> 9
<212> PRT
<213> Homo sapiens

<400> 16
Arg Asp Leu Pro Phe Phe Pro Val Asp

1 5

<210> 17
<211> 21
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(21)

<400> 17
ctg cca ttc ttc cca gtc gat 21
Leu Pro Phe Phe Pro Val Asp
1 5

<210> 18
<211> 7
<212> PRT
<213> Homo sapiens

<400> 18
Leu Pro Phe Phe Pro Val Asp
1 5

<210> 19
<211> 18
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(18)

<400> 19
ctg cca ttc ttc gtc gat 18
Leu Pro Phe Phe Val Asp
1 5

<210> 20
<211> 6
<212> PRT
<213> Homo sapiens

<400> 20
Leu Pro Phe Phe Val Asp
1 5

<210> 21
<211> 15
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(15)

<400> 21
ctg cca ttc ttc gat 15
Leu Pro Phe Phe Asp
1 5

<210> 22
<211> 5
<212> PRT
<213> Homo sapiens

<400> 22
Leu Pro Phe Phe Asp
1 5

<210> 23
<211> 12
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(12)

<400> 23
ctg cca ttc ttc 12
Leu Pro Phe Phe
1

<210> 24
<211> 4
<212> PRT
<213> Homo sapiens

<400> 24
Leu Pro Phe Phe
1

<210> 25
<211> 9
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(9)

<400> 25
cca ttc ttc 9
Pro Phe Phe
1

<210> 26
<211> 3
<212> PRT
<213> Homo sapiens

<400> 26

Pro Phe Phe
1

<210> 27

<211> 50

<212> DNA

<213> Homo sapiens

<220>

<223> Noncoding-antisense DNA

<400> 27

catgcaccag gcgtgcatgg cctcttccca ttacatctga ctctgagtga 50